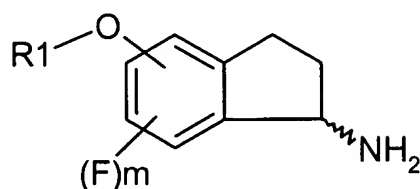


CLAIMS.

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1. A process for the preparation of an optically active substituted alpha-amino indane compound of formula (I) :

(I)



10

wherein

m is an integer selected from 0, 1, 2 and 3,

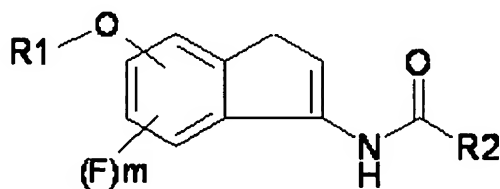
R₁ is selected from the group consisting of a hydrogen atom; an alkyl group having from 1 to 20 carbon atoms; an aryl group having from 6 to 20 carbon atoms; an alkylaryl group having from 6 to 20 carbon atoms; an alkaloyl group; and an aryloyl group,

said method comprising:

a) an asymmetric hydrogenation reaction of an en-amide compound of formula (III)

20

(III)



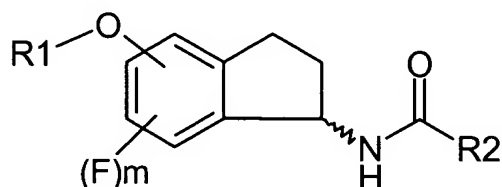
wherein m and R1 are as defined above,

R2 is selected from the group consisting of a hydrogen atom; an alkyl group having from 1 to 20 carbon atoms; an aryl group having from 6 to 20 carbon atoms; and an alkylaryl group having from 6 to 20 carbon atoms,

5 in presence of hydrogen and of an optically active catalyst,

to obtain an amide compound of formula (II) :

(II)

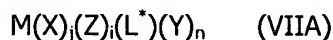


(R) ou (S)

b) a hydrolysis reaction of the amide compound of formula (II) obtained in step a),

thereby obtaining said optically active substituted alpha-amino indane compound of formula (I).

2. The process of claim 1, wherein the optically active catalyst comprises a chiral phosphine transition metal complex of formula (VIIA) :



wherein

M is a transition metal selected from the group consisting of ruthenium (Ru), rhodium (Rh) and iridium (Ir)

25 X is a halogen atom selected from the group consisting of chlorine (Cl), bromine (Br), fluorine (F) and iodine (I),

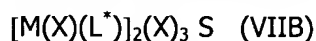
Z is selected from an aryl group having from 6 to 20 carbon atoms; an unsaturated organic group, and an unsaturated cyclic organic group, said unsaturated organic group being selected from the group consisting of an olefin, a diene and Cyano;

L* is a chiral ligand selected from the group consisting of a chiral diphosphine; a chiral atropoisomeric diphosphine, a chiral monodentate phosphoramidine, a chiral biphospholane, a chiral ferrotane and a chiral ferrocenyl phosphine,

Y is an anion selected from the group consisting of ClO_4^- ,
5 BF_4^- , PF_6^- , and SbF_6^- ,
j is an integer selected from 0 and 1,
i is an integer selected from the group consisting of 0, 1,
2 and 4,
n is an integer selected from 1 and 2.

10

3. The process of claim 2, wherein the optically active catalyst is represented by a chiral phosphine transition metal complex of formula (VIIB) :



15

Wherein:

M is a transition metal selected from the group consisting of ruthenium (Ru), rhodium (Rh) and iridium (Ir),

X is a halogen atom selected in the group consisting of chlorine (Cl), bromine (Br), fluorine (F) and iodine (I),

20

L* is a chiral ligand selected from the group consisting of a chiral diphosphine, a chiral atropoisomeric diphosphine, a chiral monodentate phosphoramidine, a chiral biphospholane, a chiral ferrotane and a chiral ferrocenyl phosphine,

S is a primary amine,

25

j is an integer selected from 0 and 1,
i is an integer selected from the group consisting of 0, 1,
2 and 4,
n is an integer selected from 1 and 2.

30

4. The process of claim 2, wherein the olefine is selected from the group consisting of pi-allyl and 1,3,5,7-cyclooctatetraene; and the diene is selected from the group consisting of 1,3-butadiene, 2,5-norbornadiene, 1,5-cyclooctadiene (COD) and cyclopentadiene.

35

5. The process of claim 1, wherein the aryl group is a benzene optionally substituted with an alkyl.

6. The process of claim 2, wherein the chiral diphosphine is selected from the group consisting of BICP, DuPHOS, MiniPHOS, BDPMI, TangPHOS, P-PHOS, Tol-P-PHOS, Xyl-P-PHOS and BPE.

5 7. The process of claim 2, wherein the chiral atropoisomeric diphosphine is selected from the group consisting of BINAP, TolBINAP, MeOBIPHEP, BINAPO, SYNPHOS and BINAPO optionally ortho-substituted with a substituent selected from an alkyl and an aryl.

10 8. The process of claim 2, wherein the chiral monodentate phosphoramidine is selected from the group consisting of Monophos and Ethylmonophos.

15 9. The process of claim 2, wherein the chiral bisphospholane is selected from the group consisting of Tangphos, Duphos, Me-Duphos Me-BPE, Et-BPE, Binaphane and Malphos.

20 10. The process of claim 2, wherein the chiral ferrocenyl phosphine is JOSIPHOS.

11. The process of claim 1, wherein the optically active catalyst is selected from group consisting of $\text{Ru}(\text{COD})(\text{MeOBIPHEP})\text{BF}_4^-$, $\text{Ru}(\text{COD})(\text{BINAP})\text{BF}_4^-$ and $\text{Rh}(\text{COD})(\text{Me-BPE})\text{BF}_4^-$.

25 12. The process of claim 1, wherein the solvent used during the assymetric hydrogenation is selected from the group consisting of an ether, and aromatic hydrocarbon, and halogenated hydrocarbon and an alcohol.

30 13. The process of claim 12, wherein the ether is selected from the group consisting of tetrahydrofuran (THF), tetrahydropyran and diethyl ether; the aromatic hydrocarbon is selected from the group consisting of benzene and toluene; the halogenated hydrocarbon is dichloromethane, the alcohol is selected from the group consisting of methanol, ethanol and isopropanol.

14. The process of claim 1, wherein the molar ratio of the enamide compound of formula (III) to the catalyst (VII) used during the asymmetric hydrogenation is ranging between 100/1 and 10000/1.

5 15. The process of claim 1, wherein the molar ratio of the enamide compound of formula (III) to the catalyst (VII) ranges between 100/1 and 1000/1

10 16. The process of claim 1, wherein the molar ratio of the enamide compound of formula (III) to the catalyst (VII) ranges between 200/1 and 1000/1.

15 17. The process of claim 1, wherein the hydrogen pressure ranges between 0,5 and 20 bars.

18. The process of claim 1, wherein the hydrogen pressure ranges between 0,5 and 10 bars.

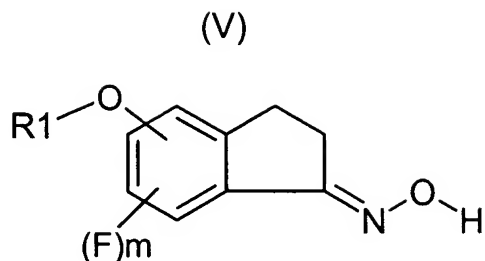
20 19. The process of claim 1, wherein the hydrogen pressure ranges between 1 and 8 bars.

20. The process of claim 1, wherein the temperature ranges between- - 20 and 100°C,

25 21. The process of claim 1, wherein the temperature ranges between- 20 and 100°C.

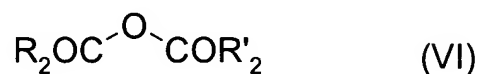
22. The process of claim 1, wherein the temperature ranges between- 20°C and 60°C.

30 23. The process of claim 1, wherein the en-amide compound of formula (III) is prepared by the two following steps :
- an acylation reaction of an alpha-hydroxyimino-indane derivative of formula (V):



wherein R_1 and m are as defined above

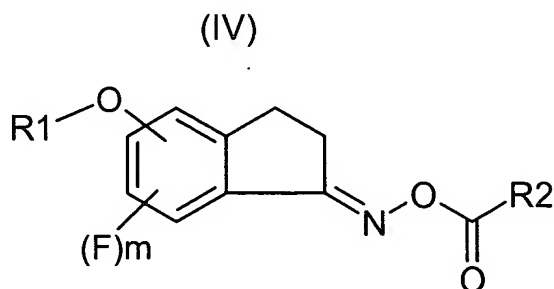
5 in presence of an organic anhydride of formula (VI) :



10 wherein R_2 and R'_2 identical or different are selected from the group consisting of a hydrogen atom, an alkyl group having from 1 to 20 carbon atoms, an aryl group having from 6 to 20 carbon atoms, and an alkylaryl group having from 6 to 20 carbon atoms,

in order to obtain an ester oxime compound of formula (IV) :

15



wherein R_1 , m and R_2 are as defined above,

20

- a hydrogenolysis-acylation reaction of the ester oxime compound of formula (IV) obtained in the previous step,

in presence of an organic anhydride of formula (VI) as defined above and of an heterogeneous catalyst comprising a transition metal selected from the group consisting of Pt, Pd, Ir, Rh and Ni,

to obtain an en-amide compound of formula (III).

5 24. The process of claim 23, wherein the molar ratio of the organic anhydride of formula (VI) to the alpha-hydroxyimino-indane of formula (V) used during the acylation reaction is ranging from 1:1 to 5:1

10 25. The process of claim 23, wherein the heterogeneous catalyst used during the hydrogenolysis-acylation reaction of the derivative of formula (IV) is selected from the group consisting of PtO₂, Pt/C, Pd/C, Pd(OH)₂/C, Ir/C, Rh/C and Raney Ni.

15 26. The process of claim 23, wherein the effective amount of the heterogeneous catalyst used during the hydrogenolysis-acylation is ranging between 0.1% and 30% for 1 mole of the ester oxime compound of formula (IV).

20 27. The process of claim 23, wherein the molar ratio of the organic anhydride of formula (VI) to the ester oxime compound of formula (IV) used during the hydrogenolysis-acylation reaction ranges between 1 : 1 and 5 : 1.

25 28. The process of claim 23, wherein the acylation reaction of the compound of formula (V) and the hydrogenolysis-acylation reaction of the compound of formula (IV) are respectively performed in an aprotic non-basic solvent selected from the consisting of an ether, and organic acid alkyl ester, an aromatic hydrocarbon and a halogenated hydrocarbon.

30 29. The process of claim 23, wherein the organic anhydride of formula (VI) used during the acylation reaction and the hydrogenolysis-acylation reaction is selected from the group consisting of a dialkyl anhydride, a diaryl anhydride and an alkylarylanhydride,

30 30 The process of claim 23, wherein the organic anhydride is acetic anhydride.

35 31. The process of claim 23, wherein the derivative of formula (III) is obtained directly from the derivative of formula (V) without isolating specifically the derivative of formula (IV).